DETAILED ACTION

The Amendment filed March 8, 2011 in response to the Office action on December 8, 2010 is acknowledged and has been entered. Claims 1, 3, 6-10, 12-13, 15-16, 25, 28, and 31-39 are pending and under examination in this Office action.

Double Patenting

The Double Patenting Warning **is withdrawn** upon further consideration.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 6-10, 12-13, 15-16, 25, 28 and 31-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1, 3, 6-10, 12-13, 15-16, 25, and 28**,** Claims are drawn to a method of removal of abnormal infective prion proteins from aqueous liquid consisting essentially of passing the liquid through a depth filter comprising a binder and kiselguhr or perlite particles having a pore size providing retention less than 6 microns (...) wherein the aqueous liquid is blood plasma product derived from plasma.

The claims are rejected because the plasma products recited in claim 13 are not by themselves aqueous liquids but proteins. The claims require the removal of abnormal infective prion proteins from aqueous liquid by passing the aqueous liquid through a filter. However the claims define the aqueous liquid as being a plasma product such as albumin, an immunoglobulin,

Factor IX, thrombin, fibronectin, fibrinogen, Factor VIII, Factor II, Factor VII, Factor IX, and Factor X. The plasma products without the plasma liquid are not aqueous but may be actually provided in form of a solid powder in case when the plasma products are freeze-dried, for example. It is not clear how the plasma products recited in the present claims form the aqueous liquid. It is not clear if Applicant intended to recite "the aqueous liquid is plasma containing plasma products". Clarification and/or correction is required.

Regarding claims 31-39, Claims are drawn to removal of abnormal infective prion proteins from plasma fraction wherein the plasma fraction consists essentially of a protein selected from the group consisting of immunoglobulins and albumin. It is noted that the phrase "consisting essentially of" typically means that the additional components are not essential for the purpose of the invention. In the present case the plasma fraction must contain the liquid part of the plasma in order to pass the liquid through the filer. The plasma fraction consisting essentially of a protein selected from the group consisting of immunoglobulins and albumin may be interpreted to mean purified immunoglobulins or albumin without the liquid plasma, which cannot be passed through the filer. Applicant is suggested to amend the claims to recite “wherein the plasma fraction contains a protein selected from the group consisting of immunoglobulins and albumin" or wherein the plasma fraction is the “immunoglobulin containing plasma fraction or albumin containing plasma fraction”. The recitation of “fraction" already indicates that either immunoglobulins or albumin are the main component of that plasma fraction.

Correction is required.

Claim Rejections - 35 USC § 102

Rejection of Claim 14 under 35 U.S.C. 102(b) as being anticipates by Brown et al. (Transfusion, 1998, Vol. 38, p. 810-816) **is moot** because Applicant canceled the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 3, 6-10, 12-13, 15-16, 25, 28 and 31-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerba et al. (Applied and Environmental Microbiology, 1985, p. 1375-1377) **in view** of Brown et al. (Transfusion, 1998, Vol. 38, p. 810-816) is maintained.

Gerba teaches method of removal of Escherichia coli and endotoxin from tap water-aqueous liquid, comprising passing the water through a 3.9 cm^2 depth filter formed of a matrix comprising a cellulose binder and kiselguhr (diatomaceous earth) (see Materials and Methods). Gerba teaches that endotoxin removal was highly effective at pH from 4.0 to 7.5 (see page 1376).

Gerba discusses the pore size however Gerba does not provide the number of the pore size. However since Gerba is using the same material in the filer, the kieselguhr and is able to retain the endotoxin particles and pass water, it would have been obvious that Gerba's filter will

retain prions and pass the liquid. It would have been within the skill of ordinary artisan to vary and adjust the pore size depending on the liquid being passed through the filer. It would have been obvious to optimize the filter pore size, the filter thickness and the filter permeability. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Gerba does not teach treating the filter with ethanol however it would have been obvious to do that for the disinfection purposes. Gerba does not teach using the filter to remove prions form blood products such plasma.

Brown teaches methods of fractionation of plasma to remove infectious prions (see Materials and Methods). Brown teaches blood plasma product subject to prion removal. Brown teaches blood plasma product albumin (see page 815).

However, it would have been *prima facie* obvious to provide the methods of removal of infectious prions from plasma taught by Brown using Gerba's depth filter comprising cellulose and kieselguhr because Gerba teaches that his depth filter allows for enhanced removal of bacteria and bacterial endotoxin from solution (see page 1375). It would have been obvious to

provide a single use filter so that any contaminants are not transferred from one plasma product to another.

All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Applicant's arguments

Applicant's arguments have been fully considered but fail to persuade. Applicant argues that Gerba teaches endotoxins which are completely different biological entity than the prions of the present invention. Applicant argues that endotoxins are a completely different and distinct biological entity than prions because they differ from each other in structure, function, and chemistry. Applicant argues that there is no teaching or suggestion in Gerba that prions are similar to endotoxins and that there is no teaching or suggestion that prions would function similarly to endotoxins in the methods described in Gerba.

Applicant argues that Gerba teaches away from the claimed invention because the removal of bacteria endotoxins by filtration, as described in Gerba, is limited to water or aqueous solutions containing small molecules (e.g., glucose, sucrose) and that Gerba reports that the removal of endotoxins from depth filters was decreased in the presence of 5% newborn calf serum. Applicant states that Gerba teaches that proteins in the serum likely compete with the

endotoxin for adsorptive sites on the filters and that "no significant removal of endotoxin was observed with negatively charged filter media." Applicant argues that Gerba teaches that removal of bacterial endotoxins by filtration would not be effective when handling complex biological solutions of proteins, such as serum. Additionally, given that proteins in serum, such as serum albumin, are negatively charged, one skilled in the art would find that Gerba teaches away from the filtration of negatively charged liquids and complex biological solutions of proteins, such as serum.

Applicant argues that Brown fails to correct the deficiencies of Gerba. Applicant argues that Brown examines the infectivity in blood components and Cohn plasma fractions in normal human blood that was "spiked" with trypsinized cells from a scrapie-infected hamster brain and in blood of clinically ill mice inoculated with a mouse-adapted strain of human transmissible spongiform encephalopathy. Applicant argues that Brown is directed towards an assessment of risk to patients receiving plasma products, not towards the planned and controlled removal of prion protein contaminants. Applicant argues that Brown fails to teach or suggest the use of filters or a filtration process. Rather, Brown describes a plasma fractionation process, which is a scaled-down approximation of the precipitation procedures used during manufacture of plasma products. Applicant argues that Brown fails to teach or suggest a reason to modify the filtration methods of Gerba, directed to the removal of endotoxins, to achieve the claimed invention.

In response to Applicant's arguments the Examiner noted that Applicant's claims 1, 3, 6-10, 12-13, 15-16, 25 and 28 do not recite passing the serum or plasma containing the infectious prion through the filer containing binder and kiselgur or perlite particles. The claims recite

passing aqueous liquid which is plasma product. The claims do not recite 1) passing plasma through the filter and 2) do not recite that the plasma contains the infectious prion. Claims 31-38 do not recite serum or plasma fraction containing the infectious prion. Applicant is also directed to the 1.112 second paragraph rejection above regarding the ambiguity of the recited plasma products. While the bacterial endotoxin and prions are different unrelated molecules, based on the teachings in Gerba and Brown the skilled artisan would conclude that it would have been obvious to try to remove infective prion from plasma product of Brown by passing the plasma product through the filter in Gerba. The Supreme Court provided a number of bases on which a claimed invention may be found obvious. One of them is "obvious to try". In particular, "When there is a design need or market pressure to solve a problem and there are a finite number of identified predictable potential solutions, a person of ordinary skill has good reason to pursue the known potential options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense" (*KSR International Co. v. Teleflex Inc.* (82 U.S.P.Q. 2d1385, 2007).

Regarding Applicant's argument about Gerba teaching away from the claimed invention, the Examiner notes that Gerba states that the presence of calf serum decreased the efficiency of endotoxin removal. Gerba does not teach the presence of serum made it impossible to remove the endotoxin or pass the solution through the filter. Because Gerba teaches using the kiselguhr filter for a wide variety of solutions and because Gerba was able to pass the calf serum through the kieselguhr filer the skiled artisan would have had a reasonable expectation of success to pass the plasma fraction containing infectious prion through the kieselguhr filter and to remove the

infectious prions. Brown teaches that plasma fractions contain infectious prion and teaches that Cohn fractionation reduces the prion infectivity to very low or undetectable levels (see page 815, right column). Based on the combined teachings of Gerba and Brown the skilled artisan would have had a reasonable expectation of success to remove the infectious prion from the plasma fraction of Brown using the method taught in Gerba that is using the kiselguhr filter.

For those reasons and because Applicant's arguments are not persuasive as discussed above, the rejection is maintained.

Conclusion

No claims are allowed.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/

Primary Examiner, Art Unit 1648